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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/376,604	08/18/1999	RAGUPATHY MADIYALAKAN	AREX-P03-004	6693

7590 09/25/2003

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EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	30

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/376,604	MADIYALAKAN ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims pending in the application are 113,115-121,123,125,128-135,137-139,141-144,170-175,177-183,185,187,190-204,206-209 and 235-239.

Continuation of Disposition of Claims: Claims rejected are 113,115-121,123,125,128-135,137-139,141-144,170-175,177-183,185,187,190-204,206-209 and 235-239.

Response to Amendment

The Amendment filed June 30, 2003 (Paper No. 29) in response to the Action mailed March 26, 2003 (Paper No. 26) is acknowledged and has been entered.

Claims 122, 124, 126-127, 136, 140, 184, 186, 188-189, and 205 were cancelled.

Claims 235-239 were added.

Claims 113, 115-121, 123,125, 128-135, 137-139, 141-144, 170-175, 177-183, 185, 187, 190-204, 206-209, 235-239 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New Rejections/Objections:

Specification

The abstract of the disclosure is objected to because the abstract is entitled "Abstract of the Invention". However, the abstract is not the abstract of the invention but is the Abstract of the Disclosure. Correction is required. See MPEP § 608.01(b).

Claim 128 is rejected under 35 USC 112, 2nd paragraph for being indefinite because it recites the phrase "native antibody". The claim is indefinite because it is unknown what a native antibody is, for example, is a native antibody one that is produced in the same organism to which

it is administered or is it one that is not altered from one produced in the same or a different organism, is it one that retains the binding site and specificity of an antibody known to bind to a specific antigen.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 113, 115-121, 123, 128, 131-135, 137-139, 141-144, 170-175, 177-183, 185, 190, 193-204, 206-209, 235-239 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 5,532,159 (Webb *et al.* April 1, 1994).

Due to the indefiniteness of the claim language, claims drawn to "native" antibodies are assumed to encompass any antibody.

US Patent No. 5,532,159 teaches a method for inducing a therapeutic host immune response against a multi-epitopic antigen that does not elicit an effective host immune response comprising contacting a multi-epitopic antigen present in the host's serum (column 10, line 55+, column 17) with a composition comprising a binding agent that specifically binds to a first epitope on the antigen, the binding agent present in the composition being non-radiolabeled, and allowing the binding agent to form a binding agent/antigen pair. Specifically, the patent teaches

monoclonal antibody therapy against a cancer cell product, oncofetal protein or "OFP". OFP, alone or in-vivo, does not elicit an effective immune response wherein the patent further teaches that OFP may be immunosuprresive (column 2, lines 55+). The patent further teaches dosages of 100μg or 165μg which reads on binding agent in an amount of from 0.1μg to 2mg per kg of body weight of the host or 1 μg to 200μg per kg of body weight of the host. Additionally, the patent teaches a murine monoclonal antibody which is an AB1 antibody (column 7, lines 65+). For examination purposes, the cloning of hybridomas expressing the AB1 antibody reads on a genetically engineered antibody. In the instant case, the effective immune response is the shrinkage of tumor cells due to administration of the antibody. Although the patent does not specifically teach that the specific immune response is elicited "against a second epitope on the antigen in the binding agent/antigen pair" (Claim 113) or elicited "against the antigen" (Claim 135) or "wherein the binding agent/antigen complex elicits an effective immune response against the mulit-epitopic in vivo antigen" (Claim 174) or that the effective immune response comprises a cellular and or humoral immune response, the method steps described in the prior art comprise the same steps as claimed in the instant invention and the claimed functional limitations would be an inherent property of the referenced method. Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Hence, even though the claims include specific immunological mechanisms, the claimed method does not appear to distinguish over the prior art teaching of the same or nearly the same method. The mechanism of action does not have a bearing on the patentability of the invention if

the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 113, 115-121, 123-125, 128-135, 137-139, 141-144, 170-175, 177-183, 185, 187, 190-204, 206-209, 235-239 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baum *et al.* (Hybridoma, Vol. 12, No. 5, 1993, pages 583-589) **or** Madiyalakan *et al.* (Hybridoma, Volume 14, No. 2, May 19, 1995) in further view of US Patent No. 5,532,159 (Webb *et al.* April 1, 1994).

Due to the indefiniteness of the claim language, claims drawn to "native" antibodies are assumed to encompass any antibody.

Baum *et al.* (and or Madiyalakan *et al.*) detail successful methods for inducing a therapeutic host immune response against a multi-epitopic in vivo antigen (CA125) that does not elicit an effective immune response comprising contacting a multi-epitopic antigen present in the

host's serum with a composition comprising a binding agent that specifically binds to a first epitope on the antigen, the binding agent present in the composition being "radiolabeled", and allowing the binding agent to form a binding agent/antigen pair whereby an effective host immune response is elicited wherein the antibody is B43.13, wherein the antigen is CA125, and wherein the level of CA125 in the host's serum is greater than 100U/ml (Baum *et al.*Table 2, Madiyalakan *et al.*, Fig. 5). Baum *et al.* further teaches dosage ranges between 0.1μg to 2mg per keg of body weight (Table 1) and that HAMA reactions were observed and appeared to be associated with increased survival of ovarian cancer patients (Figure 5, page 588) which reads on humoral immune responses. Baum *et al.* further teach, that from a clinical point of view, there is a beneficial effect on the overall well-being and perhaps the survival rate of patients with ovarian carcinomas who are receiving repeated administrations of anti-CA-125 antibodies, including B43.13 (page 588). Further, although Baum *et al.* does not characterize the type of administration or that the composition comprises one or more pharmaceutically acceptable carriers, the teachings of Baum *et al.* were retrospective in nature and one of ordinary skill in the art would appreciate that such administrations included immunologically suitable routes in solution-type compositions that included pharmaceutically acceptable carriers. Further, although there is no documented cellular immune response, the increased survival rate of cancer patients would include such a response because murine monoclonal antibodies directed against tumor associated antigens include various antitumor mechanisms such as antibody-dependent cellular cytotoxicity, complement-dependent cytolysis, and apoptosis.

Baum *et al.* (or Madiyalakan *et al.*) do not specifically teach nor suggest that the anti-CA-125 antibodies be administered in a non-radiolabeled form or a dosage from 1 μg to 200 μg per kg of body weight.

As set forth above, Webb *et al.* successfully teach the treatment of cancer with the administration of non-radiolabeled binding agents to a soluble tumor antigen, OFP. Webb *et al.* also caution against the use of conjugating antibodies to radioisotopes because of toxic side effects and that their invention provides a low-cost, less toxic anti-cancer immunotherapy which enhances the host's immune system's ability to destroy or contain cancers (column 2, lines 10 and 40).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modulate the teachings of Baum *et al.* or Madiyalakan *et al.* so as to include non-radiolabeled binding agents for the purpose of treating cancer patients. One would have been motivated to do so because Webb *et al.* caution against the use of conjugating antibodies to radioisotopes because of toxic side effects wherein their invention provides a low-cost, less toxic anti-cancer immunotherapy which enhances the host's immune system's ability to destroy or contain cancers. Moreover, one of ordinary skill in the art would have a reasonable expectation of success in using the non-radiolabeled antibodies since Webb *et al.* teach that such antibodies enhance the host's immune system's ability to destroy or contain cancers. Furthermore, with regards to optimum parameters (i.e. dosages ranging from 1 μg to 200 μg per kg of body weight), it is well within the level of ordinary skill in the art to determine optimum concentrations of reactants. See In re Kronig, 190 USPQ 425.

Rejection Re-instated:

The deposit rejection made in Paper No. 14, pages 2-3 is officially re-instated. Applicants have argued (Paper No. 15, pages 5-6) that the deposited hybridomas have been deposited with the ATCC in accordance with the provisions of the Budapest Treaty and that all restrictions upon public access were "irrevocably removed" when US Patent No. 6,241,985 was granted. This argument has been considered but is not found persuasive. The prosecution of this case is independent from the prosecution of the parent case and declarations or affidavits filed during said prosecution of the parent do not automatically become a part of this pending application. Furthermore, statements attesting to broad implications, i.e. that the provisions of the Budapest treaty are fulfilled do not satisfy the deposit rules. Applicants must file an affidavit or declaration (by applicants, assignees or a statement by an attorney of record over his or her signature and registration number) stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
September 23, 2003